Highly Stereoselective 6 π Electrocyclization of Bridged Bicyclic 1,3,5-Trienes

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Supporting Information: Experimental procedures and physical data (pages S-1–11) for **4a-h**, **6a-e,g,h**, **8d,e**, stereochemical analyses for electrocyclization products (page S11), and copies of NMR spectra (pages S-12–44; proton NMR only for **6h**).

General Information. Reactions were conducted in oven-dried (120°C) or flame-dried glassware under a positive argon atmosphere unless otherwise stated. Transfer of anhydrous solvents or mixtures was accomplished with oven dried syringes or cannulae. Solvents were distilled before use: dichloromethane (CH₂Cl₂) from calcium hydride; toluene from sodium; and tetrahydrofuran (THF) from sodiumbenzophenone ketyl. For reactions involving preparation and use of activated Zn, solvents used were of reagent grade purity and were filtered through basic alumina before use. Chloroform-*d* was filtered through basic alumina before use. Commercial reagents were used as received unless otherwise stated. Thin layer chromatography (TLC) was performed on glass plates precoated with 0.25 mm Kieselgel 60 F₂₅₄ (Merck). Flash chromatography columns were packed with 230–400 mesh silica gel (Silicycle), or ~150 mesh, 58Å, activated neutral Brockmann I, standard grade alumina (Aldrich) as indicated. Proton nuclear magnetic resonance spectra (¹H NMR) were recorded at 500 MHz, and the chemical shifts are reported on the δ scale (ppm) upfield from deuteriochloroform (δ = 7.27 ppm). Coupling constants (*J*) are reported in Hertz (Hz). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; dd, doublet of doublets, etc. Carbon nuclear magnetic resonance spectra (¹³C NMR) were obtained at 125 MHz. Chemical shifts are reported (ppm) relative to the center line of the triplet for deuteriochloroform (δ = 77.23 ppm). Infrared (IR) spectra were measured with a Mattson Galaxy Series FT-IR 3000 spectrophotometer. Mass spectra were determined on a PerSeptive Biosystems Mariner high-resolution electrospray positive ion mode spectrometer.

Preparation of Dienynes 4

Dienyne 4a. To a solution of vinyl triflate **2a**¹ (196 mg, 0.72 mmol) in THF (21 mL) and Et₂NH (21 mL) was added CuI (14 mg, 0.072 mmol), and Pd(PPh₃)₂Cl₂ (25 mg, 0.036 mmol). The mixture was flushed with argon at room temperature for 20 minutes. The alkyne **3a**² (110 mg, 0.86 mmol), dissolved in THF (2 mL), was then added via cannula and the resulting solution was heated to reflux, and stirred 12 hours. The mixture was cooled to room temperature and then concentrated directly. Purification was achieved by column chromatography using neutral alumina eluting with 100% hexanes and gave 165 mg (87% yield) of dienyne **4a** as a clear colorless oil. *R*_f 0.52 (20:1 hexanes/EtOAc); IR (CH₂Cl₂ film) 3059, 2955, 2871, 2176 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.42-7.24 (m, 5H), 6.94 (d, *J* = 16.1 Hz, 1H), 6.36 (d, *J* = 16.2 Hz, 1H), 6.32 (d, *J* = 3.3 Hz, 1H), 2.39 (dd, *J* = 3.6, 3.6 Hz, 1H), 1.92 (dddd, *J* = 12.3, 7.3, 3.7, 3.7 Hz, 1H), 1.59 (ddd, *J* = 12.0, 9.0, 3.5 Hz, 1H), 1.17-1.11 (m, 4H), 1.05 (ddd, *J* = 12.1, 9.3, 3.4 Hz, 1H), 0.84 (s, 3H), 0.82 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 141.0, 140.3, 136.6, 132.2, 128.7, 128.3, 126.2, 108.6, 92.7, 88.4, 56.5, 55.8, 52.2, 31.2, 24.9, 19.6, 19.5, 12.0; HRMS for C₂₀H₂₂ (M⁺) calcd 262.1723, found 262.1728.

Dienyne 4b. To a solution of vinyl triflate **2b**¹ (220 mg, 0.74 mmol) in THF (19 mL) and Et₂NH (19 mL) was added CuI (20 mg, 0.11 mmol), and Pd(PPh₃)₂Cl₂ (25 mg, 0.036 mmol). The mixture was flushed with argon at room temperature for 20 minutes. The alkyne **3a** (114 mg, 0.89 mmol), dissolved in THF (2 mL), was then added via cannula and the resulting solution was heated to reflux, and stirred 12 hours. The mixture was cooled to room temperature and then concentrated directly. Purification was achieved by column chromatography using neutral alumina eluting with 100% hexanes and gave 203 mg (100% yield) of dienyne **4b** as a clear colorless oil. *R*_f 0.23 (100% hexanes); IR (CH₂Cl₂ film) 3059, 2955, 2875, 2177 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.42-7.24 (m, 5H), 6.94 (d, *J* = 16.2 Hz, 1H), 6.34 (d, *J* = 16.2 Hz, 1H), 5.94 (d, *J* = 3.1 Hz, 1H), 5.02 (s, 1H), 2.32-2.23 (m, 1H), 2.17-2.12 (m, 2H), 1.84-1.77 (m, 4H), 1.11 (s, 3H), 1.08 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 140.5, 140.2, 136.9, 136.5, 134.1,

¹ Mazzola, R. D., Jr.; Giese, S.; Benson, C. L.; West, F. G. *J. Org. Chem.* **2004**, *69*, 220.

² Michel, P.; Gennet, D.; Rassat, A. *Tetrahedron Lett.* **1999**, *40*, 8575.

128.7, 128.4, 126.2, 116.6, 108.5, 92.0, 89.2, 59.0, 47.9, 44.2, 27.1, 26.8, 24.1, 20.7; HRMS for $C_{21}H_{22}$ (M^+) calcd 274.1723, found 274.1720.

Dienyne 4c. To a solution of vinyl triflate **2c**¹ (128 mg, 0.43 mmol) in THF (12 mL) and Et_2NH (12 mL) was added CuI (8 mg, 0.042 mmol), and $Pd(PPh_3)_2Cl_2$ (15 mg, 0.021 mmol). The mixture was flushed with argon at room temperature for 20 minutes. The alkyne **3a** (66 mg, 0.51 mmol), dissolved in THF (1 mL), was then added via cannula and the resulting solution was heated to reflux, and stirred 12 hours. The mixture was cooled to room temperature and then concentrated directly. Purification was achieved by column chromatography using neutral alumina eluting with 100% hexanes and gave 111 mg (94% yield) of dienyne **4c** as a clear colorless oil. R_f 0.70 (10:1 hexanes/ $EtOAc$); IR (neat) 3059, 2962, 2863, 2178 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.41-7.25 (m, 5H), 6.93 (d, $J = 16.1$ Hz, 1H), 6.34 (d, $J = 16.2$ Hz, 1H), 6.09 (d, $J = 3.3$ Hz, 1H), 4.73 (s, 1H), 2.54 (d, $J = 4.1$ Hz, 1H), 2.47 (br s, 1H), 2.04 (ddd, $J = 9.8, 4.7, 4.7$ Hz, 1H), 1.98 (d, $J = 9.9$ Hz, 1H), 1.80 (s, 3H), 1.12 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5, 138.9, 138.6, 136.4, 134.5, 128.7, 128.5, 128.4, 126.2, 108.4, 92.8, 88.6, 50.5, 48.6, 39.8, 35.1, 30.3, 25.0, 23.5; HRMS for $C_{20}H_{22}$ (M^+) calcd 274.1723, found 274.1718.

Dienyne 4d. To a solution of the alkyne **3b**³ (45 mg, 0.37 mmol) in THF (0.5 mL) at $-78^\circ C$ was added $nBuLi$ (0.225 mL, 1.6 M, 0.37 mmol). The resulting mixture was allowed to stir at this temperature for 0.5 h, whereby a solution of $ZnCl_2$ (49 mg, 0.37 mmol) in THF (0.5 mL) was added via cannula. The solution was warmed to $0^\circ C$, and left to stir for another 0.5 h. Following this, vinyl triflate **2a** (50 mg, 0.18 mmol) in THF (0.5 mL) was added via cannula, and $Pd(PPh_3)_4$ (6 mg, 0.005 mmol) was subsequently added in 1 solid portion. The mixture was warmed to room temperature and left to stir overnight. The reaction was quenched by the addition of saturated aqueous NH_4Cl (1.5 mL). The aqueous layer was extracted with Et_2O (2 x 5 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Gravity column chromatography using silica treated with 1% Et_3N /hexanes afforded 38 mg (80% yield) of dienyne **4d** as a yellow oil. R_f 0.58 (100% hexanes); IR (neat) 3060, 2956, 2873, 2179, 1556 cm^{-1} .

³ Fiandanesse, V.; Marchese, G.; Punzi, A.; Ruggieri, G. *Tetrahedron Lett.* **1996**, 37, 8455.

¹H NMR (500 MHz, CDCl₃) δ 6.41 (d, *J* = 19.2 Hz, 1H), 6.28 (d, *J* = 3.3 Hz, 1H), 6.13 (d, *J* = 19.2 Hz, 1H), 2.36 (dd, *J* = 3.6, 3.6 Hz, 1H), 1.90 (dddd, *J* = 12.1, 7.6, 3.7, 3.7 Hz, 1H), 1.56 (ddd, *J* = 12.2, 9.0, 3.5 Hz, 1H), 1.13-1.06 (m, 4H), 1.06 (ddd, *J* = 11.8, 9.3, 3.1 Hz, 1H), 0.81 (s, 3H), 0.80 (s, 3H), 0.09 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 144.5, 141.2, 132.1, 123.6, 93.6, 86.4, 56.4, 55.7, 52.2, 31.1, 24.9, 19.6, 19.5, 11.9, -1.6; HRMS for C₁₇H₂₆Si (M⁺) calcd 258.1805, found 258.1805.

4e

Dienyne 4e. To a solution of the alkyne **3b** (42 mg, 0.34 mmol) in THF (0.5 mL) at -78°C was added nBuLi (0.215 mL, 1.6 M, 0.34 mmol). The resulting mixture was allowed to stir for 0.5 h, whereby a solution of ZnCl₂ (46 mg, 0.34 mmol) in THF (0.5 mL) was added via cannula. The solution was warmed to 0°C, and left to stir for another 0.5 h. Following this, the vinyl triflate **2b** (50 mg, 0.17 mmol) in THF (0.5 mL) was added via cannula, and Pd(PPh₃)₄ (6 mg, 0.005 mmol) was subsequently added in 1 solid portion. The mixture was then heated to reflux for 2 hours. The reaction was quenched by the addition of saturated aqueous NH₄Cl (1.5 mL). The aqueous layer was extracted with Et₂O (2 x 5 mL), and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Gravity column chromatography using silica treated with 1% Et₃N/hexanes afforded 46 mg (100% yield) of dienyne **4e** as a yellow oil. *R*_f 0.52 (100% hexanes); IR (CH₂Cl₂ film) 2955, 2925, 2181, 1559 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.41 (d, *J* = 19.2 Hz, 1H), 6.15 (d, *J* = 19.2 Hz, 1H), 5.88 (d, *J* = 2.8 Hz, 1H), 4.99 (s, 1H), 2.24 (d, *J* = 16.6 Hz, 1H), 2.11 (s, 2H), 1.80-1.74 (m, 4H), 1.08 (s, 3H), 1.05 (s, 3H), 0.09 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 144.8, 140.1, 137.1, 134.0, 123.5, 116.5, 92.7, 87.2, 58.9, 47.8, 44.2, 27.2, 26.7, 24.1, 20.6, -1.6; HRMS for C₁₈H₂₆Si (M⁺) calcd 270.1805, found 270.1808.

4f

Dienyne 4f. To a solution of the alkyne **3b** (32 mg, 0.26 mmol) in THF (0.5 mL) at -78°C was added nBuLi (0.165 mL, 1.6 M, 0.26 mmol). The resulting mixture was allowed to stir for 0.5 h, whereby a solution of ZnCl₂ (35 mg, 0.26 mmol) in THF (0.5 mL) was added via cannula. The solution was warmed to 0°C, and left to stir for another 0.5 h. Following this, the vinyl triflate **2c** (50 mg, 0.17 mmol) in THF (0.5 mL) was added via cannula, and Pd(PPh₃)₄ (6 mg, 0.005 mmol) was subsequently added in 1 solid portion. The mixture was then heated to reflux for 2 hours. The reaction was quenched by the addition of saturated aqueous NH₄Cl (1.5 mL). The aqueous layer was extracted with Et₂O (2 x 5 mL), and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Gravity column chromatography using silica treated with 1% Et₃N/hexanes afforded 47 mg (100% yield) of dienyne **4f** as a yellow oil. *R*_f 0.50

(100% hexanes); IR (neat) 2957, 2864, 2183, 1597 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 6.42 (d, J = 19.2 Hz, 1H), 6.12 (d, J = 19.2 Hz, 1H), 6.05 (d, J = 3.1 Hz, 1H), 4.70 (s, 1H), 2.49 (d, J = 4.4 Hz, 1H), 2.45 (br s, 1H), 2.01 (ddd, J = 12.2, 4.3, 4.3 Hz, 1H), 1.96 (d, J = 10.7 Hz, 1H), 1.77 (d, J = 1.6 Hz, 3H), 1.10 (s, 3H), 0.86 (s, 3H), 0.09 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 144.8, 138.9, 138.4, 134.2, 128.3, 123.4, 93.5, 86.5, 50.4, 48.5, 39.6, 34.9, 30.2, 24.9, 23.3, -1.7; HRMS for $\text{C}_{18}\text{H}_{26}\text{Si}$ (M^+) calcd 270.1805, found 270.1807.

Dienyne 4g. nBuLi (130 μL , 2.4 M, 0.31 mmol) was added to a -78°C solution of diisopropyl amine (43 μL , 0.31 mmol) in THF (0.5 mL). The solution was warmed to 0°C and stirred for 20 mins before being cooled back to -78°C . The alkyne **3c**⁴ (30mg, 0.28 mmol) in THF (0.3 mL) was then cannulated into the cooled base solution and stirred at this temperature for 30 mins. Next, a THF (0.5 mL) solution of ZnCl_2 (42 mg, 0.31 mmol) was added via cannula and the mixture was warmed to 0°C and stirred for 30 mins. A solution of the vinyl triflate **2a** (50 mg, 0.18 mmol) in THF (0.3 mL) was then cannulated into the reaction mixture followed by addition of solid $\text{Pd}(\text{PPh}_3)_4$ (3 mg, 0.005 mmol). After warming to room temperature, the solution was heated to reflux until TLC showed consumption of the vinyl triflate (~ 1.5 h). The mixture was cooled to r.t. and quenched by the addition of H_2O (2.5 mL). The aqueous layer was extracted with Et_2O (2 x 5 mL), and the combined Et_2O washings were dried over anhydrous MgSO_4 , filtered, and concentrated. The crude residue was purified by flash column chromatography (neutral alumina) eluting with 50:1 hexanes/ Et_2O and gave 25 mg (57% yield) of dienyne **4g** as a colorless oil. R_f 0.5 (20:1 hexanes: EtOAc); IR (CH_2Cl_2 film) 2956, 2873, 2180, 1725, 1620, 1566 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 6.95 (d, J = 15.8 Hz, 1H), 6.44 (d, J = 3.3 Hz, 1H), 6.19 (d, J = 15.7 Hz, 1H), 3.79 (s, 3H), 2.41 (dd, J = 3.7, 3.7 Hz, 1H), 1.92 (dddd, J = 15.2, 7.8, 3.4, 3.4 Hz, 1H), 1.60 (ddd, J = 12.1, 9.2, 3.5 Hz, 1H), 1.13-0.99 (m, 5H), 0.81 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 166.5, 144.2, 131.6, 128.4, 125.8, 95.5, 90.5, 56.7, 55.9, 52.5, 51.7, 31.1, 24.6, 19.5, 19.4, 11.8; HRMS for $\text{C}_{16}\text{H}_{20}\text{O}_2$ (M^+) calcd 244.1464, found 244.1465.

Dienyne 4h. nBuLi (130 μL , 2.4 M, 0.31 mmol) was added to a -78°C solution of diisopropyl amine (43 μL , 0.31 mmol) in THF (0.5 mL). The solution was warmed to 0°C and stirred for 20 mins before being cooled back to -78°C . The alkyne **3c** (32mg, 0.29 mmol) in THF (0.3 mL)

⁴ Wei, X.; Taylor, R. J. K. *Tetrahedron Lett.* **1998**, 39, 3815.

was then cannulated into the cooled base solution and stirred at this temperature for 30 mins. Next, a THF (0.5 mL) solution of ZnCl_2 (42 mg, 0.31 mmol) was added via cannula and the mixture was warmed to 0°C and stirred for 30 mins. A solution of the vinyl triflate **2b** (50 mg, 0.17 mmol) in THF (0.3 mL) was then cannulated into the reaction mixture followed by addition of solid $\text{Pd}(\text{PPh}_3)_4$ (3 mg, 0.005 mmol). After warming to room temperature, the solution was heated to reflux until TLC showed consumption of the vinyl triflate (~ 1.5 h). The mixture was cooled to r.t. and quenched by the addition of H_2O (2.5 mL). The aqueous layer was extracted with Et_2O (2 x 5 mL), and the combined Et_2O washings were dried over anhydrous MgSO_4 , filtered, and concentrated. The crude residue was purified by flash column chromatography (neutral alumina) using a gradient elution consisting of 60:1, 50:1, 40:1, 30:1, 20:1 hexanes/ Et_2O and gave 28 mg (63% yield) of diyne **4h** as a colorless oil. R_f 0.4 (20:1 hexanes: EtOAc); IR (CH_2Cl_2 film) 2952, 2924, 2182, 1725, 1622, 1574 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 6.94 (d, J = 15.7 Hz, 1H), 6.19 (d, J = 15.8 Hz, 1H), 6.06 (d, J = 3.2 Hz, 1H), 5.00 (br s, 1H), 3.77 (s, 3H), 2.32-2.22 (m, 1H), 2.18-2.12 (m, 2H), 1.84-1.74 (m, 4H), 1.08 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 166.4, 140.1, 139.9, 133.3, 128.7, 125.6, 116.7, 96.0, 89.6, 58.7, 51.8, 48.1, 44.3, 27.0, 26.5, 24.0, 20.5; HRMS for $\text{C}_{17}\text{H}_{20}\text{O}_2$ (M^+) calcd 256.1464, found 256.1465.

Reductive Electrocyclization of Diynes: Preparation of Cyclohexadienes **6**

6a

Cyclohexadiene 6a. Activated Zn dust was prepared as described by Boland et al.⁵ Argon was bubbled through a suspension of Zn dust (1.5 g) in distilled H_2O (6 mL) for 15 mins. $\text{Cu}(\text{OAc})_2$ (0.15 g) was added and the flask was immediately sealed. The mixture was vigorously stirred for 15 mins. AgNO_3 (0.15 g) was then added, and the solution was stirred for 30 mins. The activated Zn was then filtered and washed successively with H_2O , MeOH, acetone, and Et_2O . The moist activated Zn was transferred immediately to a flask containing the reaction solvents H_2O (2 mL) and THF (1.5 mL). Compound **4a** (140 mg, 0.53 mmol) in THF (0.5 mL) was added to this mixture and was vigorously stirred at room temperature in the dark for 11 days. The Zn dust was removed by filtration on a sintered glass funnel and washed with large amounts of Et_2O and H_2O . The organic phase was separated, dried over MgSO_4 , filtered and concentrated. After purification by flash chromatography using silica gel eluting with 100% hexanes, 94 mg (67% yield) of cyclohexadiene **6a** was obtained as a yellow oil. R_f 0.38 (100% hexanes); IR (neat) 3026, 2985, 2954, 2888 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.28-7.15 (m, 5H), 6.26 (ddd, J = 9.8, 1.2, 0.6 Hz, 1H), 5.68 (dd, J = 9.7, 5.5 Hz, 1H), 5.48 (dd, J = 5.1, 3.2 Hz, 1H), 3.77 (dd, J = 12.5, 5.4 Hz, 1H), 2.91 (dd, J = 13.0, 3.1 Hz, 1H), 2.03 (d, J = 3.9 Hz, 1H), 1.94 (dddd, J = 12.0, 12.0, 4.9, 4.9 Hz, 1H), 1.64 (ddd, J = 12.3, 12.3, 3.3 Hz, 1H), 1.52-1.47 (m, 1H), 1.38 (ddd, J = 12.1, 9.1, 3.4 Hz, 1H), 0.82 (s, 3H), 0.70 (s, 3H), -0.20 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 153.7, 142.2, 130.6, 127.7, 126.2, 126.0, 124.4, 107.7, 50.3, 50.2, 50.0, 45.7, 39.8, 33.6, 31.8, 20.8, 20.1, 11.5; HRMS for $\text{C}_{20}\text{H}_{24}$ (M^+) calcd 264.1879, found 264.1876.

⁵ Boland, W.; Schroer, N.; Sieler, C.; Feigel, M. *Helv. Chim. Acta* **1987**, 70, 1025.

Cyclohexadiene 6b. Activated Zn dust was prepared as described above. Zn dust (0.5 g), distilled H₂O (3 mL), Cu(OAc)₂ (0.05 g), and AgNO₃ (0.05 g) were combined, then filtered. The moist activated Zn was transferred immediately to a flask containing the reaction solvents H₂O (2 mL) and THF (1.5 mL). Compound **4b** (21 mg, 0.076 mmol) in THF (0.5 mL) was added to this mixture and was vigorously stirred at room temperature in the dark for 6 days. The Zn dust was removed by filtration on a sintered glass funnel and washed with large amounts of Et₂O and H₂O. The organic phase was separated, dried over MgSO₄, filtered and concentrated. The crude residue was then redissolved in THF and heated to reflux for 6 hours. The mixture was concentrated under reduced pressure. After purification by flash chromatography using silica gel eluting with 100% hexanes, 11 mg (50% yield) of cyclohexadiene **6b** was obtained as a yellow oil. *R_f* 0.50 (100% hexanes); IR (CH₂Cl₂ film) 3026, 2985, 2924, 2882 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.23-7.15 (m, 5H), 6.22 (dd, *J* = 9.6, 5.1 Hz, 1H), 5.74 (dd, *J* = 9.6, 5.6 Hz, 1H), 5.66 (dd, *J* = 5.1, 3.0 Hz, 1H), 5.16 (s, 1H), 3.69 (dd, *J* = 11.8, 5.7 Hz, 1H), 3.06 (d, *J* = 12.2 Hz, 1H), 2.47-2.37 (m, 1H), 2.01 (s, 1H), 1.99-1.93 (m, 1H), 1.75 (s, 1H), 1.64 (s, 3H), 0.82 (s, 3H), -0.05 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 150.6, 140.8, 138.1, 130.8, 127.7, 126.5, 126.1, 125.6, 117.7, 110.4, 57.3, 50.2, 41.0, 40.7, 40.6, 35.8, 25.6, 22.6, 21.9; HRMS for C₂₁H₂₄ (M⁺) calcd 276.1879, found 276.1883.

Partial data for *trans*-hexatriene: slightly impure, 8 mg (36% yield); *R_f* 0.32 (100% hexanes); ¹H NMR (500 MHz, CDCl₃) δ 7.40 (d, *J* = 7.2 Hz, 2H), 7.31 (dd, *J* = 7.4, 7.4 Hz, 2H), 7.20 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.86 (dd, *J* = 15.7, 9.8 Hz, 1H), 6.58 (d, *J* = 15.4 Hz, 1H), 6.52-6.41 (m, 2H), 5.65 (d, *J* = 3.2 Hz, 1H), 5.01 (br s, 1H), 2.37 (s, 1H), 2.32-2.24 (m, 1H), 2.14-2.10 (m, 1H), 1.84-1.76 (m, 4H), 1.09 (s, 3H), 1.05 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 153.2, 140.4, 137.6, 131.7, 131.1, 130.0, 129.7, 129.4, 128.6, 127.3, 126.2, 117.2, 53.7, 47.6, 44.4, 27.7, 27.3, 24.3, 20.9.

Cyclohexadiene 6c. Activated Zn dust was prepared as described above. Zn dust (2.4 g), distilled H₂O (18 mL), Cu(OAc)₂ (0.24 g), and AgNO₃ (0.24 g) were combined, then filtered. The moist activated Zn was transferred immediately to a flask containing the reaction solvents H₂O (20 mL) and THF (15 mL). Compound **4c** (36 mg, 0.13 mmol) in THF (5 mL) was added

to this mixture and was vigorously stirred at room temperature in the dark for 2 days. The Zn dust was removed by filtration on a sintered glass funnel and washed with large amounts of Et₂O and H₂O. The organic phase was separated, dried over MgSO₄, filtered and concentrated. The crude residue was then dissolved in toluene and heated to reflux for 1.5 hours. The mixture was concentrated under reduced pressure. After purification by flash chromatography using silica gel eluting with 100% hexanes, 7 mg (20% yield) of cyclohexadiene **6c** was obtained as a yellow oil. *R_f* 0.55 (100% hexanes, ran twice); IR (CH₂Cl₂ film) 3082, 2963, 2925 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.27-7.18 (m, 5H), 6.14 (dd, *J* = 9.5, 4.9 Hz, 1H), 5.78 (dd, *J* = 9.6, 5.8 Hz, 1H), 5.67 (dd, *J* = 4.8, 2.8 Hz, 1H), 4.83 (s, 1H) 3.35 (dd, *J* = 10.2, 5.8 Hz, 1H), 3.23 (d, *J* = 8.6 Hz, 1H), 2.44 (d, *J* = 3.6 Hz, 1H), 1.62 (d, *J* = 1.4 Hz, 3H), 1.61-1.57 (m, 2H), 1.05 (s, 3H), 0.80 (s, 3H), 0.69 (ddd, *J* = 9.5, 5.3, 3.9 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 149.0, 138.4, 136.5, 129.8, 129.1, 127.8, 127.7, 126.7, 125.6, 110.0, 46.1, 44.8, 43.3, 42.6, 38.3, 34.2, 30.3, 26.0, 22.2; HRMS for C₂₁H₂₄ (M⁺) calcd 276.1879, found 276.1880.

Partial data for *trans*-hexatriene: *R_f* 0.44 (100% hexanes, ran twice); ¹H NMR (500 MHz, CDCl₃, partial data) δ 7.42-7.18 (m, 5H), 6.86 (ddd, *J* = 15.3, 7.5, 3.0 Hz, 1H), 6.58 (d, *J* = 15.3 Hz, 1H), 6.50-6.42 (m, 2H), 5.80 (d, *J* = 3.4 Hz, 1H), 4.72 (s, 1H).

Cyclohexadiene 6d. Activated Zn dust was prepared as previously described. Zn dust (4.0 g), distilled H₂O (30 mL), Cu(OAc)₂ (0.40 g), and AgNO₃ (0.40 g) were combined, then filtered. The moist activated Zn was transferred immediately to a flask containing the reaction solvents H₂O (40 mL) and THF (25 mL). Compound **4d** (78 mg, 0.30 mmol) in THF (5 mL) was added to this mixture and was vigorously stirred at 45°C in the dark for 6 days. The Zn dust was removed by filtration on a sintered glass funnel and washed with large amounts of Et₂O and H₂O. The organic phase was separated, dried over MgSO₄, filtered and concentrated. After purification by flash chromatography using alumina eluting with 1% Et₃N/hexanes, 70 mg (90% yield) of cyclohexadiene **6d** was obtained as a yellow oil. *R_f* 0.58 (100% hexanes); IR (CH₂Cl₂ film) 3027, 2955, 2899, 1663, 1583 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.81 (ddd, *J* = 9.8, 5.0, 2.0 Hz, 1H), 5.60 (dd, *J* = 9.8, 5.5 Hz, 1H), 5.28 (dd, *J* = 5.0, 3.1 Hz, 1H), 3.09 (dd, *J* = 14.1, 3.2 Hz, 1H), 2.21 (ddd, *J* = 14.0, 5.4, 2.1 Hz, 1H), 1.96 (d, *J* = 3.9 Hz, 1H), 1.87 (ddd, *J* = 16.8, 12.2, 4.0 Hz, 1H), 1.62 (ddd, *J* = 12.5, 12.5, 3.3 Hz, 1H), 1.39 (ddd, *J* = 14.5, 9.2, 5.3 Hz, 1H) 1.23 (ddd, *J* = 12.2, 9.3, 3.3 Hz, 1H) 1.08 (s, 3H), 0.92 (s, 3 H), 0.90 (s, 3H), 0.05 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 152.8, 125.7, 122.3, 108.0, 50.0, 49.9, 47.9, 47.3, 32.8, 32.6, 31.7, 22.6, 20.8, 11.7, 0.0; HRMS for C₁₇H₂₈Si (M⁺) calcd, 260.1961, found 260.1960.

Cyclohexadiene 6e. Activated Zn dust was prepared as previously described. Zn dust (2.2 g), distilled H₂O (17 mL), Cu(OAc)₂ (0.22 g), and AgNO₃ (0.22 g) were combined, then filtered. The moist activated Zn was transferred immediately to a flask containing the reaction solvents H₂O (20 mL) and THF (15 mL). Compound **4e** (42 mg, 0.16 mmol) in THF (5 mL) was added to this mixture and was vigorously stirred at 45°C in the dark for 3 days. The Zn dust was removed by filtration on a sintered glass funnel and washed with large amounts of Et₂O and H₂O. The organic phase was separated, dried over MgSO₄, filtered and concentrated. After purification by flash chromatography using alumina eluting with 1% Et₃N/hexanes, 23 mg (55% yield) of cyclohexadiene **6e** was obtained as a yellow oil. *R*_f 0.50 (100% hexanes); IR (CH₂Cl₂ film) 3092, 2953, 2927, 1656, 1578 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.82 (dddd, *J* = 9.8, 4.9, 1.7, 0.6 Hz, 1H), 5.67 (dddd, *J* = 9.7, 5.8, 0.8, 0.8 Hz, 1H), 5.49 (dd, *J* = 4.7, 3.1 Hz, 1H), 5.12-5.07 (m, 1H), 3.24 (d, *J* = 12.1 Hz, 1H), 2.35 (dddd, *J* = 17.2, 5.9, 2.5, 2.5 Hz, 1H), 2.18 (dddd, *J* = 12.5, 5.7, 1.0, 1.0 Hz, 1H), 2.07 (s, 1H), 1.85-1.76 (m, 2H), 1.62 (q, *J* = 1.5 Hz, 3H), 1.20 (s, 3H), 1.06 (s, 3H), 0.07 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 150.5, 137.5, 126.7, 123.4, 117.3, 111.1, 57.4, 48.3, 43.2, 41.3, 35.8, 32.7, 29.3, 22.5, 22.0, -0.2; HRMS for C₁₈H₂₈Si (M⁺) calcd 272.1961, found 272.1962.

Cyclohexadiene 6g. The dienyne **4g** (25 mg, 0.10 mmol) was dissolved in CH₂Cl₂ (5 mL) at r.t.. Quinoline (7 μ L, 0.06 mmol) was added, followed by Lindlar catalyst (21 mg, 5% Pd on CaCO₃ poisoned with Pb, 0.01 mmol). H₂ (balloon) was bubbled through the solution until TLC showed consumption of starting material (0.5h). The reaction vessel was then flushed with Argon, and left to stir at r.t. for 6 days to allow the cyclization to occur. Filtration through Celite[®] removed the spent catalyst, and the solution was then concentrated and purified by flash column chromatography (60:1 hexanes:Et₂O, silica treated with 1% Et₃N) to give 12 mg (45% yield) of cyclohexadiene **6g** as a yellow oil. *R*_f 0.56 (20:1 hexanes:EtOAc, ran twice); IR (CH₂Cl₂ film) 3039, 2953, 2871, 1731, 1597 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.12 (ddd, *J* = 9.8, 5.2, 1.1 Hz, 1H), 5.52 (dd, *J* = 10.2, 5.4 Hz, 1H), 5.46 (dd, *J* = 5.1, 3.0 Hz, 1H), 3.62 (s, 3H), 3.27 (ddd, *J* = 13.7, 5.4, 1.3 Hz, 1H), 2.77 (dd, *J* = 13.6, 2.8 Hz, 1H), 2.34 (d, *J* = 3.9 Hz, 1H), 1.96 (dddd, *J* = 12.0, 12.0, 4.9, 4.9 Hz, 1H), 1.68 (ddd, *J* = 12.5, 12.5, 3.5 Hz, 1H), 1.48 (ddd, *J* = 14.5, 9.3, 5.3 Hz, 1H), 1.33 (ddd, *J* = 12.3, 9.2, 3.4 Hz, 1H), 0.93 (s, 3H), 0.90 (s, 3H), 0.65 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 173.8, 153.3, 126.2, 119.7, 108.4, 51.7, 50.8, 50.7, 46.7, 45.9, 40.0, 32.8, 31.3, 20.7, 20.6, 11.8; HRMS for C₁₆H₂₂O₂ (M⁺) calcd 246.1621, found 246.1620.

Partial data for *trans*-hexatriene: R_f 0.61 (20:1 hexanes:EtOAc, ran twice); ^1H NMR (500 MHz, CDCl_3 , partial data) δ 7.31 (dd, $J = 15.1, 11.7$ Hz, 1H), 6.56-6.43 (m, 2H), 6.27 (d, $J = 3.3$ Hz, 1H), 5.85 (d, $J = 15.2$ Hz, 1H), 3.75 (s, 3H).

Cyclohexadiene 6h. The dienyne **4h** (15 mg, 0.06 mmol) was dissolved in CH_2Cl_2 (3 mL) at r.t.. Quinoline (5 μL , 0.04 mmol) was added, followed by Lindlar catalyst (15 mg, 5% Pd on CaCO_3 poisoned with Pb, 0.01 mmol). H_2 (balloon) was bubbled through the solution until TLC showed consumption of starting material (2h). The reaction vessel was then flushed with Argon, and left to stir at r.t. for 5 days to allow the cyclization to occur. Filtration through Celite[®] removed the spent catalyst, and the solution was then concentrated and purified by flash column chromatography (80:1 hexanes:Et₂O, silica treated with 1% Et₃N) to give 6mg (40% yield) of an inseparable mixture of 2:1 cyclohexadiene **6h**:*trans*-hexatriene as a yellow oil.

Partial data for **6h**: R_f 0.50 (20:1 hexanes/EtOAc, ran twice); ^1H NMR (500 MHz, CDCl_3) δ 6.11 (dd, $J = 9.2, 5.1$ Hz, 1H), 5.65 (dd, $J = 5.2, 3.1$ Hz, 1H), 5.56 (dd, $J = 10.3, 6.0$ Hz, 1H), 5.18 (br s, 1H), 3.63 (s, 3H), 3.28 (dd, $J = 12.1, 5.6$ Hz, 1H), 2.95 (d, $J = 12.5$ Hz, 1H), 2.48-2.40 (m, 1H), 2.16-2.11 (m, 2H), 1.64 (q, $J = 1.5$ Hz, 3H), 1.04 (s, 3H), 0.80 (s, 3H).

Partial data for *trans*-hexatriene: R_f 0.50 (20:1 hexanes/EtOAc, ran twice); ^1H NMR (500 MHz, CDCl_3 , partial data) δ 7.36 (dd, $J = 16.0, 11.3$ Hz, 1H), 6.70 (d, $J = 13.6$ Hz, 1H), 6.34 (dd, $J = 17.2, 11.4$ Hz, 1H), 5.90 (d, $J = 15.2$ Hz, 1H), 5.84 (d, $J = 3.3$ Hz, 1H), 5.0 (br s, 1H).

Attempted Sakurai Reactions of **4d** and **4e**—Preparation of Arenes **8d** and **8e**

General Procedure. To a solution of the aldehyde (1 eq) in CH_2Cl_2 (0.2M) at -78°C was added the Lewis acid (1 eq). The mixture was allowed to stir for 10 mins before the allylic silane (1 eq) in CH_2Cl_2 was added via cannula. The reaction was allowed to stir at this temperature until TLC showed consumption of the allyl silane (~ 20 – 120 mins). The mixture was then quenched with saturated aqueous NaHCO_3 . The aqueous layer was extracted with CH_2Cl_2 , and the combined organic extracts were dried over MgSO_4 , filtered, and concentrated. The crude reaction mixture was purified using gravity silica gel chromatography (100% hexanes).

Data for Arene **8d**: Clear colorless oil; R_f 0.50 (100% hexanes); IR (CH_2Cl_2 film) 3054, 2955, 2871, 1407 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.21 (dd, $J = 7.3, 1.2$ Hz, 1H), 7.10 (dd, $J = 7.3, 7.3$ Hz, 1H), 7.04 (dd, $J = 7.2, 1.2$ Hz, 1H), 2.93 (d, $J = 4.1$ Hz, 1H), 2.14-2.01 (m, 1H), 1.87-1.79 (m, 1H), 1.25 (s, 3H), 1.15-1.05 (m, 2H), 0.98 (s, 3H), 0.51 (s, 3H), 0.29 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 153.7, 149.7, 131.2, 130.2, 124.6, 120.1, 57.2, 53.5, 52.1, 33.2, 26.0, 20.0, 19.3, 11.6, -0.3; HRMS for $\text{C}_{17}\text{H}_{26}\text{Si}$ (M^+) calcd 258.1805, found 258.1803.

Data for Arene **8e**: Clear colorless oil; R_f 0.41 (100% hexanes); IR (CH_2Cl_2 film) 3021, 2954, 2921, 1446 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.25 (dd, $J = 9.1, 3.8$ Hz, 1H), 7.09-7.03 (m, 2H), 4.89 (br s, 1H), 2.74 (d, $J = 2.5$ Hz, 1H), 2.50 (s, 3H), 2.45 (dddd, $J = 18.0, 5.3, 2.8, 2.8$ Hz, 1H), 1.94 (dddd, $J = 17.5, 3.7, 2.0, 2.0$ Hz, 1H), 1.73 (dd, $J = 4.0, 2.3$ Hz, 3H), 1.20 (s, 3H), 0.89 (s, 3H), 0.28 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 152.2, 150.6, 139.4, 134.8, 131.3, 125.1, 121.1, 116.3, 56.1, 49.3, 44.9, 30.0, 27.4, 23.1, 21.1, 0.06; HRMS for $\text{C}_{18}\text{H}_{26}\text{Si}$ (M^+) calcd 270.1805, found 270.1800.

Basis of Stereochemical Assignments of Cyclohexadienes **6**

2D TROESY NMR experiments showed in most cases clear nOe interactions consistent only with the indicated stereochemistry. In addition, certain trends in the ^1H NMR chemical shift of bridgehead protons and methyls on the 1-carbon bridge of **6a-c** (significant upfield shifts presumably due to anisotropy from the *exo*-disposed phenyl group) gave further evidence for *exo* stereochemistry. Unclear interactions in the TROESY spectrum of **6e** precluded any concrete assignment of stereochemistry based on nOe. The stereochemistry in this case was based on analogy to **6b**. The stereochemistry of substrate **6h** was also assigned based on analogy to **6b**.

4b

4b

S-18

4e

S-20

S-22

S-24

4h

6g

S-38

S-40